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10/596,546

06/16/2006

Justin Ripper

101172-1P US

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01/28/2009

ASTRA ZENECA PHARMACEUTICALS LP  
GLOBAL INTELLECTUAL PROPERTY  
1800 CONCORD PIKE  
WILMINGTON, DE 19850-5437

EXAMINER

RAHMANI, NILOOFAR

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

01/28/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/596,546 | <b>Applicant(s)</b><br>RIPPER ET AL. |  |
|                              | <b>Examiner</b><br>NILOOFAR RAHMANI  | <b>Art Unit</b><br>1625              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 8-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 8-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>09/12/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Claims 1-5, 8-16 are currently pending in the instant application and claims 6-7 are cancelled.

#### *Priority*

2. This application was filed on 06/16/2006, and is a 371 of PCT/SE04/01939, filed on 12/20/2004, which claims priority of SWEDEN 0303542-5, filed on 12/22/2003.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

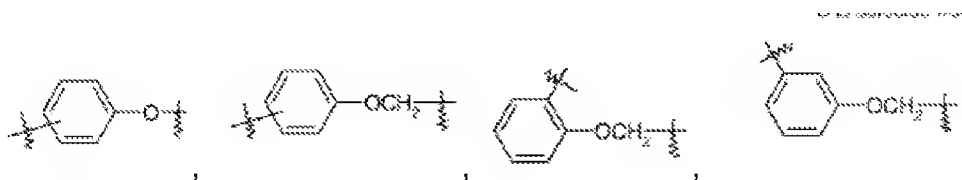
Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11-15 are rejected because the term "D is a divalent group comprising a benzene ring" is confusing. What is "a divalent group comprising a benzene ring"? Correction is required.

4. Claim 5 is rejected because the terms " 12.1.1, 12.1.2, etc." are confusing. Deletion of these words is recommended.

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5. Claims 2-4 recites the definition for "D" being phenylene, pyridylene,



. There is

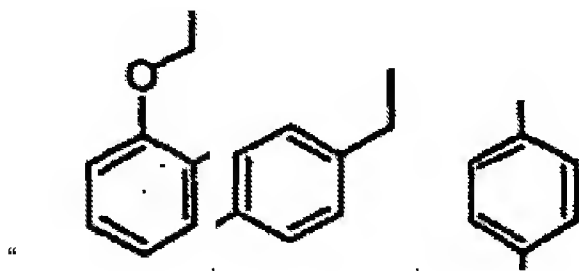
insufficient antecedent basis for this limitation in the claim.

## 6. **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 8, 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification lacks enablement of the term "D is a divalent group comprising a benzene ring", which are claimed in the compound claims. While enabling for some D being



“, which are on pages 81-158 of the

instant specification, it is not seen where this is enables for pyridylene or other types of D as a divalent group. Therefore, the specification lacks enablement for

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the term "D is a divalent group comprising a benzene ring" in the instant specification.

**7. *Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of binding of melanin concentrating hormone receptor, does not reasonably provide enablement for treat and prevent any and all diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the

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disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The nature of the invention:** The instant invention is drawn to method for the therapy of pain in a warm-blooded animal or therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective amount of a compound according to claim 1.

**The state of the prior art:** “ At the time that the invention was made, the scientific literature tends to show the speculative role of the GTP receptor and its role in the treatment of pain. “Furthermore, the binding affinity of CGRP and related peptides is modulated by nucleotides such as GTP. The cloning of various calcitonin and most recently of CGRP1 and adrenomedullin receptors was reported and revealed structural similarities but also significant differences to other members of the G protein-coupled receptors. Finally, a broad variety of biological activities has been described for CGRP-like peptides. These include vasodilation, nociception, glucose uptake and the stimulation of glycolysis in

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skeletal muscles. These effects may thus suggest their potential role and therapeutic applications in migraine, subarachnoid haemorrhage, diabetes and pain-related mechanisms, among other disorders.” (Emphasis added). ” (van Rossum D et al., Neuroscience and biobehavioral reviews, (1997 Sep) Vol. 21, No. 5, pp. 649-78. Ref: 396 Journal code: 7806090. ISSN: 0149-7634).

**The predictability in the art:** It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating a pharmacological condition in a subject.

**Amount of guidance/working examples:** Applicant provides examples of the test compounds to inhibit GTP on pages 31-39. However, There is no guidance for using a therapeutically effective amount of a compound of Formula (I) could treat any and all GTP related disease. Nor does applicant identify what diseases are treatable by therapeutically effective amount of a compound of Formula (I).

**The breadth of the claims:** The breadth of claims is drawn to method for the therapy of pain in a warm-blooded animal or therapy of functional gastrointestinal disorders in a warm-blooded animal, comprising the step of administering to said

animal in need of such therapy a therapeutically effective amount of a compound according to claim 1.

**The quantity of undue experimentation needed:** Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

**The level of the skill in the art:** The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 9-10 and 16, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NILOOFAR RAHMANI/

01/22/2009

**/D. Margaret Seaman/**

**Primary Examiner, Art Unit 1625**